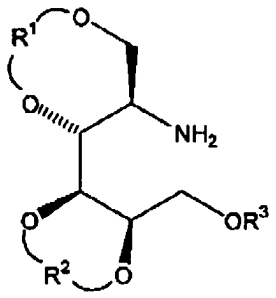
In re Appln. of Benjes et al.
Application No. 10/615,044

CLAIM AMENDMENTS

1. (Currently Amended) A process for preparing a compound of formula (I), or a salt thereof:



(I)

where R^1 and R^2 are each independently protecting groups which, together with the oxygen atoms to which they are attached, form a 5-, 6-, 7- or 8-membered ring; and R^3 is hydrogen or a protecting group;

including the steps of:

(a) protecting the hydroxyl group at the C-6 position of *N*-acetyl-D-mannosamine, to give a 6-*O*-protected-*N*-acetyl-D-mannosamine; ~~an *N*-protected-D-mannosamine, to give a 6-*O*-protected-*N*-protected-D-mannosamine;~~

(b) reducing the C-1 anomeric carbon atom of the 6-*O*-protected-*N*-acetyl-D-mannosamine to give a 6-*O*-protected-*N*-acetyl-D-mannitol; ~~6-*O*-protected-*N*-protected-D-mannosamine to give a 6-*O*-protected-*N*-protected-D-mannitol;~~

(c) protecting the four hydroxyl groups of the 6-*O*-protected-*N*-acetyl-D-mannitol; ~~6-*O*-protected-*N*-protected-D-mannitol;~~

(d) removing the nitrogen atom protecting group and optionally removing the C-6 oxygen atom protecting group to give the compound of formula (I).

2. (Cancelled)

3. (Cancelled)

4. (Original) A process according to claim 1 where R^1 and R^2, together with the oxygen atoms to which they are attached, each independently form part of a dioxane or a dioxolane ring.

5. (Original) A process according to claim 4 where R^1 and R^2 are both isopropylidene protecting groups.

6. (Currently Amended) A process according to claim 1 where the hydroxyl group at the C-6 position of the *N*-acetyl-D-mannosamine ~~*N*-protected-D-mannosamine~~ in step (a) is protected using a silylating agent.

7. (Currently Amended) A process according to claim 1 where the C-1 anomeric carbon atom of the 6-*O*-protected-*N*-acetyl-D-mannosamine ~~6-*O*-protected-*N*-protected-D-mannosamine~~ is reduced in step (b) using a metal hydride reducing agent or by hydrogenation using hydrogen gas and a metal catalyst.

8. (Currently Amended) A process according to claim 1 where 2,2-dimethoxypropane in the presence of acetone is used to protect the four hydroxyl groups of the 6-*O*-protected-*N*-acetyl-D-mannitol ~~6-*O*-protected-*N*-protected-D-mannitol~~ in step (c), to give a 1:3,4:5-di-*O*-isopropylidene-D-mannitol.

9. (Original) A process according to claim 1 where both the nitrogen atom protecting group and the C-6 oxygen atom protecting group are removed in step (d).

10. (Original) A process according to claim 1 further including the preparation of kifunensine from the compound of formula (I).

11. (Original) A process according to claim 10 including the steps of:

(e) oxamoylation of the compound of formula (I) to give a 2-oxamoylamino-D-mannitol;

(f) removal of the R^3 protecting group, where R^3 is not H;

(g) oxidation of the C-6 carbon atom to give a 2-oxamoylamino-D-mannose;

(h) double cyclisation of the 2-oxamoylamino-D-mannose to give kifunensine with four protected hydroxyl groups; and

(i) removal of the four hydroxyl protecting groups to give kifunensine.

12. (Original) A process according to claim 11 where the removal of the R^3 protecting group in step (f) is carried out after the oxamoylation step (e).

13. (Original) A process according to claim 11 where the removal of the R^3 protecting group in step (f) is carried out after the oxamoylation step (e) and before the oxidation step (g).

14. (Original) A process according to claim 11 where oxamic acid and 1,1'-carbonyldiimidazole are used for the oxamoylation of the compound of formula (I) in step (e).

15. (Original) A process according to claim 11 where the oxamoylation step (e) is a direct coupling of the compound of formula (I) with ethyl oxamate, oxalic acid mono-n-butyl ester or di-n-butyl oxalate.

16. (Original) A process according to claim 11 where pyridinium dichromate in the presence of activated molecular sieves and pyridinium trifluoroacetate is used for the oxidation of the C-6 carbon atom in step (g).

17. (Original) A process for preparing kifunensine including the steps of:

(a) silylation of *N*-acetyl-D-mannosamine using *tert*-butyldiphenylsilyl chloride as silylating agent, to give 6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-2-acetylamino-D-mannose;

(b) reduction of 6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-2-acetylamino-D-mannose using sodium borohydride as reducing agent, to give 6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-2-acetylamino-D-mannitol;

(c) protection of the four hydroxy groups of 6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-2-acetylamino-D-mannitol using 2,2-dimethoxypropane in the presence of

acetone, to give 6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-1,3:4,5-di-*O*-isopropylidene-2-acetylamino-D-mannitol;

(d) double deprotection of the 6-*O*- and *N*-protecting groups of 6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-1,3:4,5-di-*O*-isopropylidene-2-acetylamino-D-mannitol using aqueous barium hydroxide, to give 2-amino-2-deoxy-1,3:4,5-di-*O*-isopropylidene-D-mannitol;

(e) oxamoylation of 2-amino-2-deoxy-1,3:4,5-di-*O*-isopropylidene-D-mannitol using oxamic acid and 1,1'-carbonyldiimidazole, to give 2-deoxy-1,3:4,5-di-*O*-isopropylidene-2-oxamoylamino-D-mannitol;

(f) oxidation of 2-deoxy-1,3:4,5-di-*O*-isopropylidene-2-oxamoylamino-D-mannitol using pyridinium dichromate in the presence of activated molecular sieves and pyridinium trifluoroacetate, to give 5-deoxy-2,3:4,6-di-*O*-isopropylidene-2-oxamoylamino-D-mannose;

(g) double cyclisation of 5-deoxy-2,3:4,6-di-*O*-isopropylidene-2-oxamoylamino-D-mannose using a methanolic ammonia solution, to give 2,3:4,6-di-*O*-isopropylidene-kifunensine; and

(h) deprotection of 5,6:7,8-di-*O*-isopropylidene-kifunensine, using methanolic hydrochloric acid, to give kifunensine.

18. (Original) In a process for preparing kifunensine, the improvement comprising preparing kifunensine from a compound of formula (I) as defined in claim 1.